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Weber, U ; Maksymowych, W P

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PERSPECTIVE

How does imaging help the clinician in the evaluation and management of spondyloarthritis?

Ulrich Weber · Walter P. Maksymowych

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Introduction

Clinical practice and research in the field of spondyloarthritis (SpA) have changed dramatically in recent years due to the advent of magnetic resonance imaging (MRI) and the introduction of symptomatically highly effective yet expensive anti-tumor necrosis factor alpha (TNFα) agents. While physical and laboratory examinations are of limited diagnostic value, MRI is regarded as the most sensitive imaging modality for the detection of early inflammatory lesions in the axial skeleton before any inflammatory changes can be seen on standard radiography. However, plain radiography continues to play a major role in evaluating potential disease-modifying agents in the treatment of SpA.

Challenges in clinically suspected early spondyloarthritis

Diagnosing SpA at an early disease stage remains a challenge in routine practice, because physical examination has limited sensitivity, while laboratory investigation has limited specificity for this disorder. A combination of historical features has been proposed as diagnostic criteria [1], although elicitation of these historical items requires standardization and validation is necessary in primary care cohorts.

The modified New York classification criteria published in 1984 [2] are still widely used in clinical practice for making a diagnosis of ankylosing spondylitis (AS). These classification criteria rely primarily on plain radiographic features of sacroiliitis, which include erosions and sclerosis that have high disease specificity, as required for classification criteria. However, plain radiography is not helpful in most patients with clinically suspected early AS because only about 50% of patients with inflammatory back pain have developed definite radiographic features of sacroiliitis by 10 years of follow-up [3]. Hence, these criteria are not ideal for making an early diagnosis in an individual patient. Furthermore, defining reliable morphologic criteria that distinguish equivocal (stage 1) from definite (stage 2) sacroiliitis is notably difficult and is primarily quantitative. Radiographic stage 2 sacroiliitis had only modest sensitivity and specificity for AS, whether films were read by rheumatologists or radiologists, and training did not improve this [4]. Standard radiography serves primarily to confirm late-stage disease and is not suitable for early diagnosis.

In 2004, a literature review reported specificity, sensitivity, and likelihood ratios for various clinical features, laboratory findings and skeletal imaging techniques used in clinical practice for diagnosing pre-radiographic AS [5]. When clinical features of inflammatory back pain and positive HLA B27 status are present the probability of AS is estimated at 59%. The presence of inflammatory lesions on MRI is estimated to increase the probability of AS to 80–95%. The MRI studies on which these estimates were based recruited small numbers of patients with inflammatory and mechanical causes of back pain and so must be

U. Weber (✉)
Department of Rheumatology, Balgrist University Hospital,
Forchstrasse 340,
8008 Zurich, Switzerland
e-mail: ulrich.weber@balgrist.ch

W. P. Maksymowych
Department of Rheumatology, University of Alberta,
562 Heritage Medical Research Building,
Edmonton, AL T6G 2S2, Canada
e-mail: walter.maksymowych@ualberta.ca

regarded as preliminary. MR evaluation consisted largely of dynamic imaging of the sacroiliac (SI) joints with gadolinium augmentation, which is costly and therefore unlikely to be feasible in routine practice. Moreover, these estimates depend greatly on the clinical criteria used to select patients for further examination by MRI. In a cohort of 68 patients with inflammatory back pain of less than 2 years' duration, assessment of structural changes by standard radiographs, together with evaluation of inflammatory lesions on STIR sequences, was optimal for the detection of sacroiliitis [6]. However, the frequency of abnormalities detected by MRI was higher in patients meeting three sets (58%) as opposed to only one set (7%) of clinical classification criteria for SpA [7]. MRI is therefore most appropriately used in pre-radiographic disease where there is a reasonable pre-test probability based on clinical evaluation together with a positive test for HLA B27.

The second most frequent region (after the SI joints) affected by inflammation in SpA is the thoracic spine [8]. With conventional MRI the spine is imaged in the sagittal orientation in two halves, a cervicothoracic and a thoracolumbar portion. It is important to scan and evaluate the lateral portions of the thoracic spine, which include the costovertebral and costotransverse joints since one study has shown that inflammation is more common in the lateral than in the central sagittal slices [9].

The histopathological basis of bone marrow signal abnormalities seen on STIR and gadolinium-augmented sequences in SpA remains to be determined. One study demonstrated a direct correlation between the severity of histopathological abnormalities observed on CT-guided biopsies of the SI joints and the degree of gadolinium augmentation observed with dynamic MRI [10]. A recent study in 8 patients with long-standing disease undergoing spinal extension surgery showed moderate correlation between bone marrow inflammatory lesions on STIR sequences and histopathological findings of interstitial mononuclear cell infiltrates in zygapophyseal joints [11]. An MRI–histological correlation study of normal SI joints found that the synovial part of this joint is confined to the distal cartilaginous portion at the iliac side [12]. This finding may explain why early inflammatory signs on MRI of patients with clinically suspected SpA are often seen in the inferior iliac portion of the SI joints [13].

Whole body MRI is a recently introduced modification of conventional MRI that allows simultaneous assessment of the entire spine, the SI joints, the shoulder, the pelvic girdle, and the anterior chest wall in SpA [14]. Acquisition of T1-weighted spin-echo and STIR images in the coronal and sagittal planes takes 30 min to perform, which is comparable to conventional imaging. Spatial resolution is similar to that of standard MR examination. With its more comprehensive assessment of inflammation in the entire axial skeleton, whole body MRI is a promising tool for the diagnostic work-up of patients with suspected early SpA, and it may serve as an objective and quantitative measure of inflammation.

In suspected pre-radiographic SpA, computed tomography (CT) of the SI joints is no longer recommended for routine diagnostic evaluation due to the increased exposure to radiation, which is relevant to the younger SpA population. In particular, the earliest features of SpA include synovitis and capsulitis in the posterocaudal portion of the SI joints with adjacent bone marrow edema and these features are not captured on CT.

Limited studies that have compared imaging modalities have shown that bone scintigraphy of the SI joints is less sensitive than MRI in the diagnostic evaluation of inflammatory back pain [15, 16]. Its limited specificity is highlighted by the observation of increased isotope uptake in the SI joints after hopping on one leg [17]. Recent systematic literature research concluded that scintigraphy of the SI joints is of limited diagnostic value for clinically suspected early SpA [18].

The importance of MRI as the imaging method of choice for early detection of inflammation of the axial skeleton is reinforced by its inclusion in the Assessment in Ankylosing Spondylitis (ASAS) International Working Group recommendations for the management of AS [19]. However, there are still many issues that have to be clarified. We need standardized morphologic definitions for acute and chronic inflammatory lesions seen on MRI and an evaluation of their specificity and sensitivity, particularly in comparison to patients with mechanical back disorders. One of the most relevant questions for clinical practice is whether the apparently inflammatory lesions seen on MRI are indeed predictive of future structural changes visible as radiographic sacroiliitis and syndesmophyte formation. These clinically highly relevant issues have to be addressed before the radiographic sacroiliitis included in the modified New York classification criteria may be supplanted by MRI in formulating diagnostic criteria for early SpA.

Imaging in the assessment of a patient with established spondyloarthritis unresponsive to standard treatment

Clinical and laboratory evaluation are limited in their ability to discriminate between inflammatory and mechanical sources of back pain. Consequently, MRI provides additional information regarding disease activity in a patient with established AS who has failed conventional treatment. This may be particularly useful before initiating therapy with anti-TNFα agents and it may even be considered desirable to obtain a baseline MRI before committing a patient to long-term therapy with these agents.

Transdiscal fractures in an ankylosed spine (transverse fractures through intervertebral syndesmophytes, the former disk and the posterior elements of the spinal column) and transvertebral fractures may occur after minor trauma, and represent a serious complication with the risk of spinal cord injury. If the diagnosis is initially missed, these transverse spinal fractures may result in a painful intervertebral pseudarthrosis, which may be mistaken for spinal inflammatory disease activity. These fractures may be difficult to locate by standard radiography. The imaging methods of choice are CT with high resolution multiplanar reconstruction and MRI; the combination of both imaging modalities yields the highest sensitivity for detection of transverse spinal fractures [20, 21].

Osteoporosis is a common complication, not only in advanced SpA with spinal ankylosis, but may also occur early in the disease course. Loss of bone mineral density (BMD) correlates with the degree of inflammatory disease activity and improves following treatment with anti-TNFα agents [22]. Insufficiency fractures of vertebral endplates after minor trauma may be a reason for prolonged back pain. Low BMD at the femoral neck is associated with increased vertebral fracture risk in AS patients [23]. Dual energy X-ray absorptiometry screening should be considered not only in patients with spinal fusion, but also in relatively short duration disease (<10 years) if it has been marked by persistently high inflammatory activity.

Imaging in the evaluation of response to therapeutic intervention

Magnetic resonance imaging is rapidly gaining importance as an objective measure of inflammation in the spine and SI joints in AS and in complementing clinical and laboratory evaluation of disease activity, particularly because the primary validated measures of efficacy are patient self-reports. Scoring indices based on MRI have been developed that allow quantification of inflammation and are increasingly used to assess treatment response in clinical trials with the TNFα inhibitors etanercept, infliximab, and adalimumab [24–26]. An international multireader exercise evaluated three different MRI scoring methods for spinal inflammation in AS [27]. All three methods are based on the assessment of STIR sequences of the spine imaged in the sagittal plane. Two of the methods (Berlin score; AS spinal MRI activity [ASspiMRIa] score) score inflammatory lesions in a single sagittal slice, while the third method (Spondyloarthritis Research Consortium of Canada [SPARCC]) scores lesions in consecutive sagittal slices permitting three-dimensional assessment of the extent of the lesion. Feasibility and discriminatory capacity were comparable for all three scoring systems, but greater reliability was observed with the SPARCC method. The SPARCC group has also developed a scoring index for quantification of inflammation in the SI joints. A recently published randomized controlled trial of adalimumab in active AS used MRI to assess disease activity both in the spine and in the SI joints with the SPARCC methodology. The SPARCC indices were shown to be reliable and highly discriminatory between treatment groups, reinforcing their value in the clinical trial assessment of new treatment approaches [26].

At present, the suspicion of early axial SpA is mainly based on clinical grounds. There is increasing evidence that the recent advances in MRI will become essential in routine care for patients with suspected SpA to enable an earlier diagnosis of this potentially disabling disorder. In routine clinical practice STIR and T1-weighted spin-echo sequences are sufficient. Contrast-enhanced images are costly and have not been shown to offer any advantages. Imaging of the spine should be included in diagnostic protocols for SpA to ensure the evaluation of the costovertebral joints. MRI is also valuable in clinical care of patients with established SpA unresponsive to standard treatment, because it may not be possible to distinguish differing pathologies on clinical grounds alone. Monitoring the response to treatment in SpA by MRI is a focus of interest in clinical research because most efficacy measures are based on patient self-reports.

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References

1. Rudwaleit M, Khan MA, Sieper J. The challenge of diagnosis and classification in early ankylosing spondylitis. Do we need new criteria? Commentary. Arthritis Rheum 2005; 52: 1000–1008.
2. Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. Arthritis Rheum 1984; 27: 361–368.
3. Mau W, Zeidler H, Mau R, et al. Clinical features and prognosis of patients with possible ankylosing spondylitis. Results of a 10-year followup. J Rheumatol 1988; 15: 1109–1114.
4. Van Tubergen A, Heuft-Dorenbosch L, Schulpen G, et al. Radiographic assessment of sacroiliitis by radiologists and rheumatologists: does training improve quality? Ann Rheum Dis 2003; 62: 519–525.
5. Rudwaleit M, van der Heijde D, Khan MA, et al. How to diagnose axial spondyloarthritis early. Ann Rheum Dis 2004; 63: 535–543.
6. Heuft-Dorenbosch L, Landewé R, Weijers R, et al. Combining information obtained from magnetic resonance imaging and

conventional radiographs to detect sacroiliitis in patients with recent onset inflammatory back pain. Ann Rheum Dis 2006; 65: 804–808.
7. Heuft-Dorenbosch L, Landewé R, Weijers R, et al. Performance of various criteria sets in patients with inflammatory back pain of short duration; the Maastricht early spondyloarthritis clinic. Ann Rheum Dis 2007; 66: 92–98.
8. Baraliakos X, Landewé R, Hermann KG, et al. Inflammation in ankylosing spondylitis: a systematic description of the extent and frequency of acute spinal changes using magnetic resonance imaging. Ann Rheum Dis 2005; 64: 730–734.
9. Maksymowych WP, Rennie WJ, Dhillon SS, et al. Is the costo-vertebral joint the primary site of inflammation in the thoracic spine of patients with ankylosing spondylitis? Arthritis Rheum 2006; 54(Suppl 9): S474.
10. Bollow M, Fischer T, Reisshauer H, et al. Quantitative analyses of sacroiliac biopsies in spondyloarthropathies: T cells and macrophages predominate in early and active sacroiliitis—cellularity correlates with the degree of enhancement detected by magnetic resonance imaging. Ann Rheum Dis 2000; 59: 135–140.
11. Appel H, Loddenkemper C, Grozdanovic Z, et al. Correlation of histopathological findings and magnetic resonance imaging in the spine of patients with ankylosing spondylitis. Arthritis Res Ther 2006; 8: R143.
12. Puhakka KB, Melsen F, Jurik AG, et al. MR imaging of the normal sacroiliac joint with correlation to histology. Skeletal Radiol 2004; 33: 15–28.
13. Bollow M, Hermann KGA, Biedermann T, et al. Very early spondyloarthritis: where the inflammation in the sacroiliac joints starts. Ann Rheum Dis 2005; 64: 1644–1646.
14. Weber U, Pfirrmann CWA, Kissling RO, et al. Whole body MR imaging in ankylosing spondylitis: a descriptive pilot study in patients with suspected early and active confirmed ankylosing spondylitis. BMC Musculoskelet Disord 2007; 8: 20.
15. Blum U, Buitrago-Tellez C, Mundinger A, et al. Magnetic resonance imaging (MRI) for detection of active sacroiliitis—a prospective study comparing conventional radiography, scintigraphy, and contrast enhanced MRI. J Rheumatol 1996; 23: 2107–2115.
16. Yu W, Feng F, Dion E, et al. Comparison of radiography, computed tomography and magnetic resonance imaging in the detection of sacroiliitis accompanying ankylosing spondylitis. Skeletal Radiol 1998; 27: 311–320.
17. Braun J, Sieper J, Bollow M. Imaging of sacroiliitis. Clin Rheumatol 2000; 19: 51–57.
18. Song IH, Carrasco JA, Rudwaleit M, et al. The diagnostic value of scintigraphy in assessing sacroiliitis in ankylosing spondylitis and patients with clinically probable sacroiliitis—a systematic literature research [abstract]. Arthritis Rheum 2007; 56: S475.
19. Zochling J, van der Heijde D, Burgos-Vargas R, et al. ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2006; 65: 442–452.
20. Koivikko MP, Kiuru MJ, Koskinen SK. Multidetector computed tomography of cervical spine fractures in ankylosing spondylitis. Acta Radiol 2004; 7: 751–759.
21. Wang YF, Teng MMH, Chang CY, et al. Imaging manifestations of spinal fractures in ankylosing spondylitis. Am J Neuroradiol 2005; 26: 2067–2076.
22. Marzo-Ortega H, McGonagle D, Jarret S, et al. Infliximab in combination with methotrexate in active ankylosing spondylitis: a clinical and imaging study. Ann Rheum Dis 2005; 64: 1568–1575.
23. Jun JB, Joo KB, Her MY, et al. Femoral bone mineral density is associated with vertebral fractures in patients with ankylosing spondylitis: a cross-sectional study. J Rheumatol 2006; 33: 1637–1641.
24. Baraliakos X, Brandt J, Listing J, et al. Outcome of patients with active ankylosing spondylitis after two years of therapy with etanercept: clinical and magnetic resonance imaging data. Arthritis Rheum 2005; 53: 856–863.
25. Braun J, Landewé R, Hermann KGA, et al. Major reduction in spinal inflammation in patients with ankylosing spondylitis after treatment with infliximab. Results of a multicenter, randomized, double-blind, placebo-controlled magnetic resonance imaging study. Arthritis Rheum 2006; 54: 1646–1652.
26. Lambert RG, Salonen D, Rahman P, et al. Adalimumab significantly reduces both spinal and sacroiliac joint inflammation in patients with ankylosing spondylitis. A multicenter, randomized, double-blind, placebo-controlled study. Arthritis Rheum 2007; 56: 4005–4014.
27. Lukas C, Braun J, van der Heijde D, et al. Scoring inflammatory activity of the spine by magnetic resonance imaging in ankylosing spondylitis: a multireader experiment. J Rheumatol 2007; 34: 862–870.